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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/558,576	04/26/2000	Jeffrey A. Whitsett M.D.	CHMC7.001CP1	9558

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EXAMINER	
SCHNIZER, HOLLY G	
ART UNIT	PAPER NUMBER
1653	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No. 09/558,576	Applicant(s) WHITSETT M.D., JEFFREY A.
	Examiner Holly Schnizer	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,8,10 and 29-34* is/are pending in the application.

4a) Of the above claim(s) *4-6 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Status of the Claims

The Amendment and Response (Paper No. 12) filed 3-28-02 has been entered and considered.

Claims 4-6, 8, 10, and 29-34 are now pending.

Claims 4-6 and 8 are withdrawn from further consideration as being drawn to a non-elected invention.

Claims 10 and 29-34 have been examined on the merits in this Office Action.

Declaration

The Declaration under 37 C.F.R. 1.132 by Jeffrey Whitsett filed March 12, 2002 (Paper No. 13) has been considered (see obviousness rejection below for discussion).

Rejections Withdrawn

The rejection of Claims 10 and 30-32 under 35 U.S.C. 102(e) as being anticipated by Taeusch (U.S. Pat. No. 6,180,142) is withdrawn in light of Applicants' arguments.

The rejection of Claims 10 and 29-34 under 35 U.S.C. 103(a) as being unpatentable over Taeusch in view of Ariizumi et al. (U.S. Patent No. 6,046,158) is withdrawn in light of Applicant's arguments.

Rej ctions Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 30-32, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Johansson et al. (Eur. Respir. J. (1994) 7: 372-391).

Applicants argue that Johansson et al. teaches human surfactant containing surfactant proteins, non-surfactant proteins, and lipids isolated from amniotic fluid and therefore, Johansson et al. does not disclose "isolated, purified, or recombinant SP-D protein". This argument has been considered but is not deemed persuasive because, as stated in the previous Office Action, Johansson et al. teach *isolating* surfactant that contains SP-D. Thus, the SP-D protein of Johansson et al. is considered to be isolated from its natural environment. Moreover, the claims are drawn to a pharmaceutical composition *comprising* an SP-D protein and are open to include additional components including proteins and lipids, as is evidenced in claims 29-33. Absent evidence to the contrary the pharmaceutical composition of Johansson et al. is patentably indistinguishable from the claimed composition comprising an isolated, purified, or recombinant SP-D protein.

As stated in the previous Office Action, Johansson et al. review the structure and molecular biology of surfactant proteins and their role in clinical use. Johansson et al.

state "[h]uman surfactant, isolated from amniotic fluid by sucrose gradient centrifugation, as described by HALLMAN et al. [293], has been used mainly in Finland and California. It contains, apart from lipids, approximately 6% proteins, including hydrophilic (SP-A, SP-D, and nonsurfactant proteins), and hydrophobic polypeptides (SP-B, SP-C)" (see p. 381, paragraph 2). Therefore, it appears that Johansson et al. meet the limitations of the claims and the rejection is maintained.

Claims 10, 30-32, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Jobe et al. (Am. Rev. Respir. Dis. (1987) 136: 1256-1275).

Applicants argue that Jobe et al. only teaches human surfactant from amniotic fluid and does not comprise "isolated, purified, or recombinant SP-D protein". This argument has been considered but is not deemed persuasive for the following reasons. As explained above, Jobe et al. teach *isolating* surfactant that contains SP-D. Thus, the SP-D protein of Jobe et al. is considered to be isolated from its natural environment. Moreover, the claims are drawn to a pharmaceutical composition *comprising* an SP-D protein and are open to include additional components including proteins and lipids, as is evidenced in claims 29-33. Absent evidence to the contrary the pharmaceutical composition of Johansson et al. is patentably indistinguishable from the claimed composition comprising an isolated, purified, or recombinant SP-D protein.

As stated in the previous Office Action, Jobe et al. review the characteristics of surfactants and their use in the treatment of respiratory distress syndrome (RDS). Jobe et al. teach that human surfactant from amniotic fluid (which inherently contains SP-D,

SP-A, SP-B, SP-C) has been used in clinical trials for the treatment of RDS (see p. 1269, Col. 1-2, "*Human Surfactant from Amniotic Fluid*" and p. 1267, Table 5). Thus, it appears that Jobe et al. anticipate the claims and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10 and 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. (Eur. Respir. J. (1994) 7: 372-391) in view of Jain-Vora et al. (Infection and Immunity (Sept. 1998) 66(9): 4229-4236).

Applicants arguments that neither reference teaches an isolated, purified, or recombinant SP-D protein, but only teach SP-D in admixture with other surfactant proteins in amniotic fluid or surfactant and that the Johansson et al. disclosure would not motivate the skilled artisan to isolate any one of the individual ingredients of the surfactant for pharmaceutical use has been considered but is not deemed persuasive for the following reasons. The claims are drawn to a pharmaceutical composition *comprising isolated*, purified, or recombinant SP-D protein in admixture with a pharmaceutically acceptable excipient. Because the claims use the transitional language "comprising" they are open to include SP-D and any number of other components including other proteins or lipids and do not require that SP-D be isolated

individually. Moreover, the claims read on any isolated SP-D protein in water because water is considered a pharmaceutically acceptable excipient. Thus, as explained above, Johansson et al. teach *isolating* surfactant that contains SP-D. Thus, the SP-D protein of Johansson et al. is considered to be isolated from its natural environment.

Applicants argument that there would be no motivation to use isolated, purified, or recombinant SP-D as a pharmaceutical is not persuasive for the following reasons. First, Johansson et al. teach that a pharmaceutical composition *comprising* isolated SP-D (human surfactant containing SP-A, SP-B, SP-C, and SP-D isolated from amniotic fluid) has indeed been used in the clinical setting (see p. 381, Col. 2, paragraph 2). Thus, the issue in the present rejection under 35 U.S.C. 103a is not whether or not it would be obvious to make or use a pharmaceutical composition comprising SP-D since Johansson et al. anticipates (and thus makes obvious) such a composition. The present issue is whether or not a pharmaceutical composition comprising both SP-D and IL-4 would be obvious to one of ordinary skill in the art at the time of the invention. As stated in the previous Office Action and repeated below, it appears that such a composition is obvious over the prior art. Second, "Something which is old does not become patentable upon the discovery of a new property" (see MPEP 2112). While the knowledge that a composition consisting of SP-D alone is effective in suppressing the inflammatory response may be new as indicated by the Declaration by Jeffrey Whitsett (Paper No. 13), compositions "comprising" isolated SP-D are very well known in the art and have been used in pharmaceutical applications as evidenced by Johansson et al. In addition, compositions comprising "purified" and recombinant SP-D are also well

known (as evidenced by Strong et al. below) and the claimed compositions appear to be patentably indistinguishable from those of the prior art.

The Declaration under 35 CFR 1.132 by Jeffrey Whitsett (Paper No. 13) and the argument that Johansson et al. teach away from the present invention have been considered. The declaration and arguments are all directed to whether or not it would be obvious to one of skill in the art at the time of the invention to use a composition comprising SP-D as a pharmaceutical agent. The same reasoning applied above can be applied to these arguments. Most importantly, in view of the present claims, the issue in the present rejection under 35 U.S.C. 103a is not whether or not it would be obvious to make or use a pharmaceutical composition comprising SP-D since Johansson et al. anticipates (and thus makes obvious) such a composition. The present issue is whether or not a pharmaceutical composition comprising both SP-D and IL-4 would be obvious to one of ordinary skill in the art at the time of the invention. It appears that such a composition is unpatentable over the prior art as explained below. Applicants argument that Claims 29 and 33 are patentable because they include all of the limitations of the claims from which they depend is not persuasive for the reasons stated above and for the reasons stated in the previous Office Action and repeated below.

As stated in the previous Office Action, Johansson et al. teach a pharmaceutical composition comprising SP-A, SP-B, SP-C, and SP-D (see p. 381, paragraph 2) and an excipient. Johansson et al. also teach that SP-D and SP-A play a role in the host-defense system of the lung (p. 377, Col. 1, last 3 lines of first paragraph). Johansson

et al. suggest that exogenous surfactant preparation my influence the response to replacement therapy in babies with pneumonia (p. 382, col. 2, 2nd paragraph, line 4-7) and points to a study showing that natural surfactant extract and human amniotic fluid (containing SP-A, SP-B, SP-C, SP-D as discussed on p. 381, second paragraph of Johansson et al.) instilled into the airways of bacterially infected newborn rabbits prevents an increase in bacterial proliferation as compared to a control not receiving the surfactant (p. 382, Col. 2, lines 13-15).

Jain-Vora et al. teaches that IL-4 is involved in bacterial host defense system by enhancing pulmonary clearance of bacteria (see title and p. 4230, last lines of Introduction). Jain-Vora et al. teaches that surfactant proteins, SP-A and SP-D also play an important role in host defense against bacterial pathogens by stimulating macrophage chemotaxis and enhancing binding of bacteria to macrophages (p. 4234, Col. 2, 2nd paragraph). The Jain-Vora et al. suggest that IL-4 protection from bacterial infection was conferred independently from SP-A and SP-D (p. 4234, Col. 2, last sentence of second paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to improve the pharmaceutical composition of Johansson et al. containing the surfactant proteins by adding IL-4 since both are well known to be important in clearance of bacteria from the respiratory tract. One of ordinary skill at the time of the invention would have been motivated to modify the composition of Johansson et al. by adding IL-4 because Jain-Vora et al. teach that IL-4 protection is independent from that of the surfactant proteins and thus it would have been expected

that addition of IL-4 to the surfactant composition of Johansson et al. would further enhance the efficacy of the composition. Thus, the claimed invention appears to be unpatentable over the prior art.

New Rejections Necessitated by Amendment

The Amendment to Claim 10 in Paper No. 12, adds the limitation that the claimed composition comprises "isolated, purified, or recombinant SP-D protein". Thus, the following are additional prior art references that provide evidence that compositions comprising specifically purified SP-D proteins that are patentably indistinguishable from that of the claimed composition were very well known in the art at the time of the invention. Both references are given as prior art since the SP-D proteins described therein appear to be purified by different methods.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Lu et al. (Biochem. J. (1992) 284: 795-802).

Lu et al. teach the purification of human SP-D from amniotic fluid and bovine SP-D from lung lavage by affinity chromatography (see abstract and p. 796, Col. 1, Materials and Methods). The composition comprising the purified SP-D described by Lu et al. contains water thus the SP-D protein of the Lu et al. composition is considered to be admixed with a "pharmaceutically acceptable excipient". Since the purified SP-D

protein of Lu et al. would be expected to have the same amino acid sequence, structure, and function as a recombinant SP-D protein, the Lu et al. composition is considered patentably indistinguishable from compositions containing recombinant SP-D proteins. Thus, absent evidence to the contrary, the presently claimed composition is patentably indistinguishable from that of Lu et al.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Inoue et al. (U.S. Patent No. 5,670,328).

Inoue et al. teach a pharmaceutical composition comprising human purified SP-D and a physiological saline solution (a pharmaceutically acceptable excipient) (see Col. 9, lines 24-26 and lines 32-35). Since the purified SP-D protein of Inoue et al. would be expected to have the same amino acid sequence, structure, and function as a recombinant SP-D protein, the Inoue et al. composition is considered patentably indistinguishable from compositions containing recombinant SP-D proteins. Thus, absent evidence to the contrary, the pharmaceutical composition of Inoue et al. appears to be patentably indistinguishable from the composition of Claim 10.

Conclusions

Related art cited in previous Office Action but not relied upon:

McCormack (Sem. Respir. Crit. Care Med. (1995) 16(1): 29-38) is an additional reference that provides evidence that SP-D is contained in amniotic fluid (p. 35, Col. 2,

lines 10-12) and that skilled artisans at the time of the invention were well aware that surfactant proteins such as those presently claimed could be used as pharmaceutical compositions in the treatment of RDS and bacterial infections such as pneumonia (p. 36, Col. 2, lines 4-9).

No Claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Mon. & Thurs., 8am-5:30pm and Tues. & Wed. 9-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

Holly Schnizer
May 29, 2002

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